REMARKS

The Office Action mailed October 2, 2007 has been carefully considered and the following response prepared.

Claims 1-36 are pending in the application. Claims 8, 13-22, 29 and 33-36 are withdrawn from consideration. Claim 1 has been amended to add the temperature range -30°C to +60°C, and claims 5 and 26 have been canceled without prejudice. New claims 39 and 40 have been added. Claims 39 and 40 are directed to the method of claim 1 wherein the reaction is carried out at a temperature of 0°C to +50°C or +10°C to +40°C, respectively. Support for the amendment to claim 1 and new claims 39 and 40 can be found throughout the specification and in particular at page 5, lines 4-10 and original claim 5. No new matter has been added.

Applicants' representative, Liza D. Hohenschutz, would like to thank Examiner Andrew Kosar for the very helpful and courteous telephone interview on February 6, 2008 during which the rejections in the Office Action mailed October 2, 2007 and proposed amendments to the claims were discussed. The substance of the interview will be discussed in more detail in connection with Applicants' response to the pertinent rejections.

Specification/Sequence Compliance

Applicants were advised that the amendment to the paragraph beginning at page 10, line 34 does not include a sequence identifier for the sequence Gly-Phe-Leu-Gly shown in the paragraph. The Office Action also includes a Notice to Comply with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

The paragraph beginning at page 10, line 34 has been amended to insert SEQ ID NO: 1. The application now complies with 37 CFR 1.821-1.825. Withdrawal of this objection to the specification is respectfully requested.

Rejections under 35 USC 103

At page 3 of the Office Action, the Examiner rejected claims 1-7, 12, 23-28 and 30-32 under 35 USC 103 as unpatentable over Smales et al., *Journal of Chemical Education*, Vol. 76, No. 11, pages 1558-1560, 1999, in view of Schäfer, Swiss patent CH-640 511, Saha et al, *Tetrahedron Letters*, Vol. 36, No. 21, pages 3635-3638 (1995) and Mimura, U.S. Patent No. 6,197,998. At page 5 of the Office Action, the Examiner rejected claims 1-7, 9-12, 23-28 and 30-32 under 35 USC 103 as unpatentable over Smales et al., Journal of Chemical Education, Vol. 76, No. 11, pages 1558-1560, 1999, in view of Schäfer, Swiss patent CH-640 511, Saha et al, *Tetrahedron Letters*, Vol. 36, No. 21, pages 3635-3638 (1995) and Mimura, U.S. Patent No. 6,197,998, and further in view of Anteunis (U.S. Patent 4,723,645).

Applicants traverse these rejections. Both rejections were discussed during the telephone interview with Examiner Kosar on February 6, 2008. During the telephone conference, Schäfer, Swiss patent CH-640 511 was discussed, and Applicants' representative proposed amending claim 1 to add the temperature range -30°C to +60°C to overcome the rejection. Examiner Kosar advised Applicants' representative that such an amendment would likely overcome the rejection, subject to a further review of the prior art, as the product of the method of claim 1 could be considered an unexpected result when the reaction was run at lower temperatures than Schäfer, Swiss patent CH-640 511. Addition of dependent claims to other temperature ranges was also discussed.

Claim 1 has been amended to state that the reaction is carried out at a temperature of -30°C to +60°C. Claims 2-4, 6-7, 9-12, 23-28 and 30-32 depend directly or indirectly from claim 1. New claims 39 and 40 are directed to the method of claim 1 wherein the reaction is carried out at a temperature of 0°C to +50°C or +10°C to +40°C, respectively.

As discussed at pages 1 and 2 of the specification, the methods of the invention make it possible to obtain, with a high preparative yield, complex peptides exhibiting several stereogenic centers, while at the same time avoiding racemization. The peptides produced by the claimed methods exhibit high optical purity.

There is no disclosure or suggestion in the combined teachings of the cited references of methods of that can produce peptides comprised of at least two enantiopure amino acids and glycine, as claimed by Applicants.

Smales et al. discloses the peptide Gly-Phe-Leu-Gly and its synthesis using a method that is different than the claimed methods, as noted by the Examiner. Smales et al. is not relevant to the claimed methods. Smales et al. does not disclose any of the steps of the claimed methods.

Schäfer discloses synthesis of trishydroxymethylmethane-substituted lower peptides. In the method disclosed therein, trishydroxymethylaminomethane is reacted with N-(2-haloacetylated) amino acids or N-(2-haloacetylated) di-, tri- and tetrapeptides of the formula X-CH_2-C(O)-Y, where X is Cl, Br or I, and Y is an amino acid or a di-, tri- or tetrapeptide. Example 3 of Schäfer discloses preparation of Tris-Gly-Gly-Arg-Ser-Threo. In Example 3, N-2-Br-acetyl-l-gly-l-arg-d-asp-l-threo (K salt) is with mixed with trishydroxymethylaminomethane and heated to boiling under reflux with exclusion of light for 45 minutes. The stereochemistry of the product, Tris-Gly-Gly-Arg-Ser-Threo, is not mentioned. The method in Schäfer appears to produce a different product than the claimed methods. The absence of any mention of the stereochemistry of the product in Example 3 also leads persons skilled in the art to believe the process results in racemization of the peptide.

Saha et al. discloses synthesis of N-linked-glycopeptoids. In Scheme 2, N-substituted glycine building blocks were prepared from t-butyl bromoacetate to which was added a primary amine to form leucine, phenylalanine and alanine analogues. Dipeptoid units were formed by coupling the glycine building blocks with an N-acetylglucosamine substituted amine. Some of the steps of the synthetic scheme were carried out at 0°C. The dipeptoid unit was further elongated by treatment with acid. Saha et al. is also not relevant to the claimed methods. The methods in Saha et al. produce a peptoid based on glycine that has no chiral centers, rather than a peptide as produced by the claimed methods.

Mimura discloses synthesis of glycyl-tyrosine using chloroacetyltyrosine and aqueous ammonia (Example 2, column 5). The reaction was carried out at a temperature of 40°C. There is no disclosure or suggestion in Mimura of preparing longer peptides.

In summary, there is no disclosure or suggestion in the combined teachings of the claimed method for preparing a peptide or a peptide derivative comprising at least two enantiopure amino acids and at least one glycine molecule. Smales et al. and Saha et al. are not relevant to the claimed methods. The method of Schäfer is carried out at a much higher temperature than the claimed methods, and appears to produce a different product than the claimed methods. There is no indication of how the process in Mimura could be used to produce enantiopure peptides, or whether it would even be possible to produce enantiopure peptides using the method disclosed in Example 2 of Mimura. The methods of the invention make it possible to obtain, with a high preparative yield, complex peptides exhibiting several stereogenic centers, while at the same time avoiding racemization. Claims 1-4, 6-7, 12, 23-28, 30-32 and new claims 39-40 are therefore not obvious in view of the combined teachings of Smales et al., Schäfer, Saha et al. and Mimura.

Anteunis et al. is concerned with the preparation of peptides that uses a coupling reaction wherein the amino acid reactants are activated with trialkylsilanes that facilitate the formation of peptide bonds. Claims 9 and 11 refer to activating agents. The step recited in claim 9 for preparing the compound of formula (II) is a separate step and not performed at the same time or as part of the step of the method of claim 1. The compound of formula (II) is a reactant in the method of claim 1. Anteunis et al. is not relevant to the method of claim 1. Anteunis et al. therefore adds nothing to the teachings of Smales et al., Schäfer, Saha et al. and Mimura that would render obvious the methods of claims 1-4, 6-7, 9-12, 23-28, 30-32, and new claims 39-40.

Claims 1-4, 6-7, 12, 23-28, 30-32, and new claims 39-40 are not obvious over the combined teachings of Smales et al., Schäfer, Saha et al. and Mimura. Claims 1-4, 6-7, 9-12, 23-28, 30-32, and new claim 39-40 are not obvious over the combined teachings of Smales et al., Schäfer, Saha et al., Mimura, and Anteunis. Withdrawal of both section 103 rejections is respectfully requested.

In view of the above, the present application is believed to be on a condition ready for allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 03-2775, under Order No. 05129-00072-US. A duplicate copy of this paper is enclosed.

Respectfully submitted,

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